

Applicants will submit a terminal disclaimer upon an indication of allowable subject matter.

## **II. The Rejection of Claims 24-29 and 32-34 under 35 U.S.C. 112**

Claims 24-29 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, "because the specification is enabling for a method practiced with a polypeptide **having a known amino acid sequence**, and for a variant product of a native peptide having a known amino acid sequence."

Claims 24-39 have been rewritten as claims 40-55 to address this rejection. Applicants therefore submit that this rejection has been overcome.

## **III. The Rejection of Claims 24, 25, 30 and 39 under 35 U.S.C. 112**

Claims 24, 25, 30 and 39 are rejected under 35 U.S.C. 112 as being indefinite. The Office Action provided several grounds for this rejection.

Claims 24-39 have been rewritten as claims 40-55 to address this rejection. Applicants therefore submit that this rejection has been overcome.

## **IV. The Rejection of Claims 24 and 32 under 35 U.S.C. 102**

Claims 24 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Luo et al. (1988, Virology, Vol. 163, pp. 341-348). This rejection is respectfully traversed.

Luo et al. disclose the study of the differences among a number of spontaneous, random changes in the viral coat protein.

However, Luo et al. do not modify a parent peptide, and therefore do not modify one or more epitopes of the parent peptide, as claimed herein.

Moreover, Luo et al. describe methods that identify protein variants of viral coat proteins which are less refractory to inhibition of their function (binding to receptor proteins involved in infection) by one or more monoclonal antibodies. Luo et al. do not disclose or suggest that these viral proteins will have a lower immunogenic response in animals.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

**V. The Rejection of Claims 24 and 32 under 35 U.S.C. 102**

Claims 24 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Keil et al. (1989, Virology, Vol. 170, pp. 392-407). This rejection is respectfully traversed.

Keil et al. disclose methods to identify subsets of a protein sequences of two serotypes of a viral coat protein, to which the members of a set of monoclonal antibodies bind. These subsets are eliminated by construction of truncated or chimeric molecules, which result in less binding to the monoclonal antibodies.

However, Keil et al. do not disclose methods to produce protein variants which evoke a lower immunogenic response in animals.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

**VI. The Rejection of Claims 24 and 32 under 35 U.S.C. 102**

Claims 24 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Choo et al. (1988, Human Immunology, Vol. 21, pp. 209-219). This rejection is respectfully traversed.

Choo et al. disclose the study of differences of different allelic forms of the HLA-B27 protein.

However, Choo et al. do not disclose modifying one or more epitopes of a parent peptide, as claimed herein.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

**VII. The Rejection of Claims 25-27, 30, 31, 33-35 and 39 under 35 U.S.C. 103**

Claims 25-27, 30, 31, 33-35 and 39 are rejected under 35 U.S.C. 103 as being unpatentable in view of any one of Choo et al., Keil et al., or Luo et al. in view of Baxter et al. (U.S. Patent No. 5,258,287), Greenfield et al. (U.S. Patent No. 4,894,443), Hopp et al. (1981, Proceedings of the National Academy of Sciences, U.S.A., Vol. 78, pp. 3824-2828), Zachariae et al. (1981, Allergy, Vol. 36, pp. 513-516) and Favre et al. (1989, Molecular Immunology, Vol. 26, pp. 17-25). This rejection is respectfully traversed.

As discussed above, the methods described in Keil et al., Choo et al., and Luo et al. do not teach or suggest methods of modifying one or more epitopes of a parent peptide to produce a protein variant that evokes a lowered immunogenic response in animals.

Baxter et al. disclose DNA coding for insulin-like growth factor. However, Baxter et al. do not teach or suggest methods of producing a protein variant by modifying one or more epitopes of a parent peptide, wherein the variant evokes a lower immunogenic response in animals, as claimed herein.

Greenfield et al., disclose polypeptides useful in the construction of conjugates between antibodies and peptide toxins. However, Greenfield et al. also do not teach or suggest methods of producing a protein variant by modifying one or more epitopes of a parent peptide, wherein the variant evokes a lower immunogenic response in animals, as claimed herein.

Favre et al. disclose in vitro binding studies on recombinant human  $\gamma$ -interferon- (IFN- ) using monoclonal antibodies.

However, Favre et al. also do not teach or suggest methods of producing a protein variant by modifying one or more epitopes of a parent peptide, wherein the variant evokes a lower immunogenic response in animals, as claimed herein.

Hopp et al. disclose methods for locating protein antigenic determinants by analyzing amino acid sequences in order to find the point of greatest local hydrophilicity.

However, Hopp et al. do not disclose methods of mapping epitopes using proteochemical and immunological methods.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

#### **VIII. The Rejection of Claim 36 under 35 U.S.C. 103**

Claim 36 is rejected under 35 U.S.C. 103 as being unpatentable in view of any one of Choo et al., Keil et al., or Luo et al. in view of Baxter et al., Greenfield et al., and Hopp et al., and further in view of Ruttenberg et al. (U.S. Patent No. 3,903,068). This rejection is respectfully traversed.

Claim 36 has been cancelled without prejudice or disclaimer. Therefore, this rejection is rendered moot.

#### **IX. The Rejection of Claims 37 and 38 under 35 U.S.C. 103**

Claims 37 and 38 are rejected under 35 U.S.C. 103 as being unpatentable in view of any one of Choo et al., Keil et al., or Luo et al. in view of Baxter et al., Greenfield et al., and Hopp et al., and further in view of Fulton et al. (U.S. Patent No. 4,970,300).

Claims 37 and 38 have been cancelled without prejudice or disclaimer. Therefore, this rejection is rendered moot.

#### **X. The Rejection of Claims 28, 29 and 34 under 35 U.S.C. 103**

Claims 28, 29 and 34 are rejected under 35 U.S.C. 103 as being unpatentable in view of any one of Choo et al., Keil et al., or Luo et al. in view of Baxter et al., Greenfield et al., Hopp et al., and Zachariae et al., and further in view of Nielsen et al. (U.S. Patent No. 4,560,651). This rejection is respectfully traversed.

Choo et al., Keil et al., Luo et al., Baxter et al., Greenfield et al., and Hopp et al. are discussed above.

Zachariae et al. disclose detergent enzymes and observations on sensitization during the production of the protease ESPERASE.

However, Zachariae et al. do not teach or suggest methods of producing a protein variant by modifying one or more epitopes of a parent peptide, wherein the variant evokes a lower immunogenic response in animals, as claimed herein.

Nielsen et al. disclose a *Bacillus* amylase.

Nielsen et al. do not teach or suggest methods of producing a protein variant by modifying one or more epitopes of a parent peptide, wherein the variant evokes a lower immunogenic response in animals, as claimed herein.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 103. Applicants respectfully request reconsideration and withdrawal of the rejection.

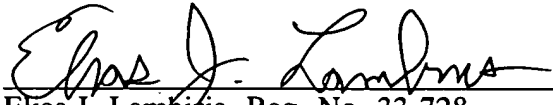
#### **XI. Conclusion**

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to

contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

Date: February 22, 2001

A handwritten signature in black ink, appearing to read "Elias J. Lambiris", written over a horizontal line.

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